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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/487,023	01/19/2000	Parkash S. Gill	21327-701 CIP	2622

7590 05/17/2002

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EXAMINER
MCGARRY, SEAN

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 05/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/487,023	Applicant(s) GILL ET AL.	
	Examiner Sean McGarry	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 9, 11, 13, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,801,156].

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1, 9, 11, 13, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,710,136].

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1, 9, 11, 13, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Uchida et al [US 6,150, 092].

Uchida et al disclose many antisense oligonucleotides that are targeted to the same target region those antisense disclosed in the instant specification and embraced in the instant claims and it is assumed that the antisense of Uchida et al inherently posses the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example. See Tables 1 and 2, for example.

Claims 1, 9, 11, 13, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al [US 5,814,620].

Robinson et al disclose several antisense oligonucleotides targeted to VEGF. It is assumed that antisense molecules of Robinson et al inherently possess the ability to inhibit at the conditions recited in the claims without evidence to the contrary. It is noted that inhibitory concentrations vary based on modifications to antisense oligonucleotides as taught in the reference, for example.

Claims 1-3, 7-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchida et al (above) and Robinson et al [5,814,620; 5,710,136; and, 5,801,156].

The claimed invention is antisense oligonucleotides for the inhibition of VEGF where there are several specific antisense sequences recited in the claims.

Robinson et al is relied upon as above and is relied upon to demonstrate that antisense oligonucleotides have been know for use in various methods of treatment prior to applicants invention and that it was known to use liposome formulations for pharmaceutical preparations of antisense oligonucleotides (see column 9, for example). It has been taught by Robinson et al that synthetic oligonucleotides of their invention [VEGF antisense] may be used in pharmaceutical preparation when combined with appropriate carrier. It is further taught that such compositions can include other factors and/or agents which enhance inhibition of VEGF expression or which will reduce neovascularation (see columns 8 and 9, for example).

Uchida et al have taught methods of inhibiting VEGF with antisense oligonucleotide. The antisense oligonucleotides claimed by Uchida et al are targeted, for example, to the specific region of VEGF nucleic acid SEQ ID NO: 7. All of the specifically recited antisense oligonucleotides of instant claim 2, for example, are all targeted to SEQ ID NO: 7 or Uchida et al, and further all the recited antisense oligonucleotides of instant claim 2 either overlap, embrace, or are embraced by the specifically claimed antisense of Uchida et al claim 7, for example (SEQ ID NOS: 51, 54, 53, 50, 49, 138, and 141 of Uchida et al, for example).

One in the art would clearly have had motivation to make the instantly claimed antisense molecules since it is absolutely clear that the region targeted has been clearly shown by the prior art to be a desired target for antisense inhibition of VEGF. Furthermore the specific antisense claimed are not only targeted to the taught target sequence but overlap, embrace or are embraced by the specific VEGF antisense taught by Uchida et al. One in the art would clearly look to these specific regions to make antisense oligonucleotides to inhibit VEGF since these specific region and antisense have been clearly taught in the art to be effective antisense oligonucleotides and target sequences. One would expect that the inhibition conditions recited in the claims would be met since these values were observed upon making antisense targeted to the specific region clearly taught in the prior art.

The invention as a whole would therefore have been prima facie obvious to one in the art at the time the invention was made.

Claims 4-6 rejected under 35 U.S.C. 103(a) as being unpatentable over Uchida Robinson et al [US 5,814,620] Barleon et al [Blood Vol. 87, No. 8:3336-3343, 4/15/96] and Chan et al [The American journal of Surgical Pathology Vol. 22(7):816-826, 1998].

Uchida et al is relied upon as above and further for the following: It has been taught at column 1, for example, that ". . .inhibition of the vascular endothelial growth factor leads to inhibition of growth of solid tumor cells, and this should be applicable in the development of anticancer agents. [I]n fact there is a report on a method to use an anti-VEGF antibody"

Robinson et al is relied upon as above and for the following: It has been taught by Robinson et al that synthetic oligonucleotides of their invention [VEGF antisense] may be used in pharmaceutical preparation when combined with appropriate carrier. It is further taught that such compositions can include other factors and/or agents which enhance inhibition of VEGF expression or which will reduce neovascularation (see columns 8 and 9, for example).

Barleon et al taught inhibition of VEGF via specific antiserum and the role of flt-1 with VEGF biopathway.

Chan et al have taught the Association of VEGF and its receptors and their roles in various diseases.

It would have been obvious to use antibodies in conjunction with antisense targeted to VEGF since the prior art has taught antisense to inhibit VEGF, antibodies to inhibit VEGF and since the art has taught that VEGF receptors are associated with the same disease sates as VEGF. The art has taught that one in the art can combine other

VEGF inhibitors in combination with VEGF antisense. Since the art has shown inhibition of VEGF by antisense and via antibodies one in the art would have a reasonable expectation of the successful use of a combination of such a combination.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SRM
May 16, 2002

SEAN McGARRY
PRIMARY EXAMINER
1635